

IN THE CLAIMS:

Claims 3, 19, 33, 40, 43, 48, 55, and 56 are canceled herein. Claims 4-7, 10-16, 18, 20, 21, 23-25, 29-31, 34-37, 41, 42, 47, 49, 50, 52, 53, 58, and 61 have been amended herein. All of the pending claims 1, 2, 4-18, 20-32, 34-39, 41, 42, 44-47, 49-54, and 57 through 66 are presented below. This listing of claims will replace all prior versions and listings of claims in the application. Please enter these claims as amended.

Listing of the Claims:

1. (Original) A pharmaceutical composition for the treatment of an inflammatory disease comprising:

a water-soluble polymer and an effective amount of an anti-inflammatory therapeutic agent linked to said water-soluble polymer, wherein the water-soluble polymer specifically accumulates in sites of inflammation.

2. (Original) The pharmaceutical composition of claim 1, further comprising a targeting moiety linked to the water-soluble polymer.

3. (Canceled).

4. (Currently amended) The pharmaceutical composition of ~~claims 1, 2 or 3~~ claim 1, wherein the water-soluble polymer is selected from the group consisting of a HPMA copolymer, polyethylene glycol, polyglutamic acid, polyaspartic acid, dextran, chitosan, cellulose, starch, gelatin, hyaluronic acid and derivatives thereof.

5. (Currently amended) The pharmaceutical composition of ~~any one of claims 1-4~~ claim 1, further comprising a bio-assay label linked to the water-soluble polymer.

6. (Currently amended) he pharmaceutical composition of ~~any one of claims 1-5~~ claim 1, further comprising a spacer between the therapeutic agent and the water-soluble polymer, wherein the spacer is cleavable.

7. (Currently amended) The pharmaceutical composition of ~~any one of claims 1-5~~ claim 1, further comprising a spacer between the therapeutic agent and the water-soluble polymer, wherein the spacer is uncleavable.

8. (Original) The pharmaceutical composition of claim 1, wherein the anti-inflammatory therapeutic agent is a glucocorticoid.

9. (Original) The pharmaceutical composition of claim 2, wherein the targeting moiety directs the composition to bone or cartilage.

10. (Currently amended) The pharmaceutical composition of claim 2 ~~or claim 9~~, wherein the targeting moiety is selected from the group consisting of bisphosphonates, quaternary ammonium groups, peptides, oligo-Asp, oligo-Glu, aminosalicic acid, antibodies and fragments or derivatives thereof.

11. (Currently amended) The pharmaceutical composition of ~~claims 2, or 9-10~~ claim 2, wherein the link between the targeting moiety and the water-soluble polymer is cleavable.

12. (Currently amended) The pharmaceutical composition of ~~claims 2, or 9-10~~ claim 2, wherein the link between the targeting moiety and the water-soluble polymer is uncleavable.

13. (Currently amended) The pharmaceutical composition of ~~any one of claims 1-11~~ claim 1, wherein the water-soluble polymer comprises N-(2-hydroxypropyl)methacrylamide.

14. (Currently amended) The pharmaceutical composition of ~~any one of claims 1-3 and 5-12~~ claim 1, wherein the water-soluble polymer comprises one or more monomers selected from the group consisting of, N-(2-hydroxypropyl)methacrylamide, N-isopropyl-acrylamide, acrylamide, N,N-dimethylacrylamide, N-vinylpyrrolidone, vinyl acetate, 2-methacryloxyethyl glucoside, acrylic acid, methacrylic, vinyl phosphonic acid, styrene sulfonic acid, maleic acid, 2-methacryloxyethyltrimethylammonium chloride, methacrylamidopropyltrimethylammonium chloride, methacryloylcholine methyl sulfate, N-methylolacrylamide, 2-hydroxy-3-methacryloxypropyltrimethyl ammonium chloride, 2-methacryloxyethyltrimethylammonium bromide, 2-vinyl-1-methyl-pyridinium bromide, 4-vinyl-1-methylpyridinium bromide, ethyleneimine, (N-acetyl) ethyleneimine, (N-hydroxyethyl)ethyleneimine, allylamine and combinations thereof.

15. (Currently amended) The pharmaceutical composition of ~~any one of claims 1-7 and 9-14~~ claim 1, wherein the therapeutic agent is selected from the group consisting of proteins, peptides, NSAIDs, DMARDs, glucocorticoids, methotrexate, sulfasalazine, chloriquine, gold, gold salt, copper, copper salt, penicillamine, D-penicillamine, cyclosporine, and mixtures thereof.

16. (Currently amended) A method for the treatment of an inflammatory disease comprising:

administering a the pharmaceutical composition of claim 1 to a subject thought to have an inflammatory disease, ~~wherein the composition comprises a water soluble polymer and an effective amount of a therapeutic agent linked to said water soluble polymer~~; and

accumulating the pharmaceutical composition in inflamed tissue of the subject by the affinity of the water-soluble polymer for the inflamed tissue.

17. (Original) The method according to claim 16, further comprising targeting the water-soluble polymer to a specific tissue.

18. (Currently amended) The method according to ~~of claims~~ claim 16 or 17, wherein the inflammatory disease comprises rheumatoid arthritis.

19. (Canceled).

20. (Currently amended) The method according to ~~any of claims 16-19~~, claim 16, further comprising: conducting a biodistribution assay wherein the composition is labeled.

21. (Currently amended) The method according to ~~any of claims 16-20~~ claim 16, further comprising cleaving the link between the therapeutic agent and the water-soluble polymer.

22. (Original) The method according to claim 17, wherein targeting the water-soluble polymer to a specific tissue comprises targeting bone or cartilage.

23. (Currently amended) The method according to ~~claims 17 or 19~~ claim 17, wherein targeting the water-soluble polymer to a specific tissue comprises using a targeting moiety selected from the group consisting of bisphosphonates, quaternary ammonium groups, peptides, oligo-Asp, oligo-Glu, aminosalicyclic acid, antibodies and fragments or derivatives thereof.

24. (Currently amended) The method according to claims 17, ~~or 23~~, further comprising cleaving ~~the~~ a link between the targeting moiety and the water-soluble polymer.

25. (Currently amended) A method of administering an aqueous composition to a subject, said method comprising:

administering ~~a~~ the pharmaceutical composition of claim 1 in an aqueous solvent or diluent to a subject thought to have rheumatoid arthritis; and

allowing accumulation and targeting of the pharmaceutical composition in an arthritic joint, thereby improving a treatment of arthritis.

26. (Original) The method according to claim 25, further comprising reducing a side effect of the therapeutic agent in tissues other than the arthritic joint.

27. (Original) The method according to claim 25, wherein the therapeutic agent is selected from the group consisting of a NSAIDs, DMARDs, cyclooxygenase-2 inhibitor, a glucocorticoid, a tumor necrosis factor blocker and an interleukin-1 receptor antagonist.

28. (Original) The method according to claim 25, wherein the water-soluble agent comprises a HPMa copolymer.

29. (Currently amended) A composition for imaging and ~~evaluation of~~ evaluating an inflammatory disease comprising:

a water-soluble polymer and an effective amount of a medical imaging agent linked to said water-soluble polymer, wherein the medical imaging agent is used in the imaging and evaluation of an inflammatory disease.

30. (Currently amended) The composition of claim 29, further comprising ~~an effective amount of~~ a therapeutic agent linked to said water-soluble polymer.

31. (Currently amended) The composition of claim 29 ~~or 30~~, wherein the medical imaging agent is selected from the group consisting of at least one of a MRI, PET, CT and γ -scintigraphy agent.

32. (Original) The composition of claim 29, further comprising a targeting moiety linked to the water-soluble polymer.

33. (Canceled).

34. (Currently amended) The composition of ~~claims 29, 30, 31, 32 or 33~~ claim 29, wherein the water-soluble polymer is selected from the group consisting of ~~a~~ an HPMA copolymer, polyethylene glycol, polyglutamic acid, polyaspartic acid, dextran, chitosan, cellulose, starch, gelatin, hyaluronic acid and derivatives thereof.

35. (Currently amended) The composition of ~~any one of claims 29-34~~ claim 29, further comprising a bio-assay label linked to the water-soluble polymer.

36. (Currently amended) The composition of ~~any one of claims 29-35~~ claim 29, further comprising a spacer between the imaging agent and the water-soluble polymer, wherein the spacer is cleavable.

37. (Currently amended) The composition of ~~any one of claims 29-35~~ claim 29, further comprising a spacer between the imaging agent and the water-soluble polymer, wherein the spacer is uncleavable.

38. (Original) The composition of claim 30, further comprising a spacer between the therapeutic agent and the water-soluble polymer, wherein the spacer is cleavable.

39. (Original) The composition of claim 30, further comprising a spacer between the therapeutic agent and the water-soluble polymer, wherein the spacer is uncleavable.

40. (Canceled).

41. (Currently amended) The composition of claim ~~40~~ 32, wherein the targeting moiety directs the composition to bone or cartilage.

42. (Currently amended) The composition of claim ~~40~~ 32, wherein the targeting moiety is selected from the group consisting of bisphosphonates, quaternary ammonium groups, peptides, oligo-Asp, oligo-Glu, aminosalicyclic acid, antibodies and fragments or derivatives thereof.

43. (Canceled).

44. (Original) The composition of claim 29, wherein the water-soluble polymer comprises N-(2-hydroxypropyl)methacrylamide.

45. (Original) The composition of claim 29, wherein the water-soluble polymer comprises one or more monomers selected from the group consisting of N-(2-hydroxypropyl)methacrylamide, *N*-isopropylacrylamide, acrylamide, *N,N*-dimethylacrylamide, *N*-vinylpyrrolidone, vinyl acetate, 2-methacryloxyethyl glucoside, acrylic acid, methacrylic, vinyl phosphonic acid, styrene sulfonic acid, maleic acid, 2-methacryloxyethyltrimethylammonium chloride, methacrylamido-propyltrimethylammonium chloride, methacryloylcholine methyl sulfate, *N*-methylolacrylamide, 2-hydroxy-3-methacryloxypropyltrimethyl ammonium chloride, 2-methacryloxyethyltrimethylammonium bromide, 2-vinyl-1-methylpyridinium bromide, 4-vinyl-1-methylpyridinium bromide, ethyleneimine, (*N*-acetyl)ethyl-eneimine, (*N*-hydroxyethyl)ethyleneimine, allylamine and combinations thereof.

46. (Original) The composition of claim 30, wherein the therapeutic agent is selected from the group consisting of proteins, peptides, NSAIDs, glucocorticoids, methotrexate, sulfasalazine, chloriquine, gold, gold salt, copper, copper salt, penicillamine, D-penicillamine, cyclosporine, and mixtures thereof.

47. (Currently amended) A method for imaging and evaluation of an inflammatory disease in a subject, the method comprising:

administering the ~~imaging agent~~ composition of claim 29 to the subject; and

imaging an inflammatory disease patient or animal model before and after the administration of the imaging agent with MRI, PET, CT or γ -scintigraphy equipment.

48. (Canceled).

49. (Currently amended) The method according to ~~claims 47 or 48~~ claim 47, further comprising conducting a biodistribution assay.

50. (Currently amended) The method according to claim 47, ~~48 or 49~~, further comprising targeting the water-soluble polymer to a specific tissue.

51. (Original) The method according to claim 50, wherein targeting of the compound is directed to bone or cartilage.

52. (Currently amended) The method according to ~~claims 50 or 51~~ claim 50, wherein targeting the compound to a specific tissue comprises using a targeting moiety selected from the group consisting of bisphosphonates, quaternary ammonium groups, peptides, oligo-Asp, oligo-Glu, aminosalicic acid, antibodies and fragments or derivatives thereof.

53. (Currently amended) The method according to ~~any one of claims 50-52~~ claim 50, further comprising cleaving a link between the targeting moiety and the water-soluble polymer.

54. (Original) The method according to claim 50, wherein imaging an inflammatory disease patient or animal model enhanced with the compound comprises imaging an arthritic joint.

55. - 56. (Canceled).

57. (Original) The pharmaceutical composition of claim 1, wherein the therapeutic agent comprises a plurality of distinct therapeutic agents.

58. (Currently amended) The pharmaceutical composition of ~~claims 2, 8 or 9~~ claim 2, wherein the targeting moiety comprises a plurality of distinct targeting moieties.

59. (Original) The pharmaceutical composition of claim 58, wherein the plurality of distinct targeting moieties target a plurality of tissues.

60. (Original) The pharmaceutical composition of claim 5, wherein the bio-assay label comprises a plurality of distinct bio-assay labels.

61. (Currently amended) The pharmaceutical composition of claim 6 ~~or claim 7~~, wherein the spacer comprises a plurality of chemically distinct spacers.

62. (Original) The composition of claim 31, wherein the imaging agent comprises a plurality of distinct imaging agents.

63. (Original) The method according to claim 55, wherein the imaging agent comprises at least two imaging agents, wherein each of the two imaging agents is used in a different imaging technique.

64. (Original) A composition comprising a water-soluble N-(2-hydroxypropyl) methacrylamide copolymer linked to a targeting moiety and to a glucocorticoid via a pH sensitive hydrozone bond.

65. (Original) The composition of claim 64, wherein the glucocorticoid is dexamethasone.

66. (Original) The composition of claim 64, wherein the targeting moiety is hydrazine.